REMARKS

Elections/Restrictions

The Examiner found Applicant's proposed modification of the election of species requirement persuasive. SEQ ID NOs:1-3, 6 and 7 are being examined. Claims 16, 18-20, 22-25, 27-33, 35 and 36 are readable on this combination of oligonucleotides. See page 2, lines 7-10, of the Office Action.

Substitute Sequence Listing

A Substitute Sequence Listing is being filed concurrently herewith. The Substitute Sequence Listing will replace all previous versions of Sequence Listings. The Substitute Sequence Listing corrects an inadvertent typographical error in the previously filed Sequence Listings. Specifically, the last nucleotide in SEQ ID NO:6 has been deleted therefrom. The letter "T" denotes TAMRA (carboxytetramethylrhodamine) label, not deoxythymidine. Accordingly, the second last nucleotide in SEQ ID NO:6 has become the last nucleotide therein, with a TAMRA label added as a "feature" of the sequence, and is, therefore, represented by the letter "n" in the Substitute Sequence Listing.

The specification has also been amended to correct this inadvertent typographical error accordingly. No new matter has been added.

Amendments to the Specification

The specification was objected to because of informalities.

The Examiner stated: "The specification recites nucleic acid sequences greater than 10 nucleotides in length that are not identified by the appropriate SEQ ID NO: at pages 6-10, 14, 15, 17, and 19." The Examiner also stated: "The 'Brief Description of the Drawings' heading is missing." See page 3, lines 6-8, of the Office Action.

The specification has been amended to identify the nucleic acid sequences greater than 10 nucleotides in length at pages 6-10, 14, 15, 17, and 19 by their appropriate SEQ ID NOs. The specification has also been amended to add the "Brief Description of the Drawings" heading.

Appropriate corrections required by the Examiner have been made, thereby rendering the objections to the specification moot.

Amendments to the Claims

Claims 11, 16, 18-20 and 30 have been amended to more clearly define Applicant's invention. New Claims 38-40 have been added.

Support for the amended and the new claims can be found throughout the specification as filed, e.g., at page 4, lines 1-3, page 6, lines 11, 15, 25 and 26, and page 8, line 21, of the specification as filed. Entry is respectfully requested.

Rejection of Claims 18-20, 35 and 36 under 35 U.S.C. § 101

Claims 18-20, 35 and 36 were rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter.

The Examiner stated: "The claims are directed to products of nature, specifically nucleic acids." The Examiner suggested that "[a]mendment of the claims to indicate that the claimed oligonucleotide primers and probes are 'isolated and purified' would overcome this rejection." See page 3, lines 16-18, of the Office Action.

Claims 18 and 19 have been amended to indicate that the claimed oligonucleotide primers and probes are "isolated and purified," as suggested by the Examiner. Claims 18 and 19, as amended, meet the requirement under 35 U.S.C. § 101.

Claim 20 is directed to an oligonucleotide comprising the sequence of SEQ ID NO:6. Claim 35 is directed to an oligonucleotide comprising SEQ ID NO:7. SEQ ID NOs:6 and 7 each have at least one nucleotide artificially modified and thus are not products of nature. Claim 36 is directed to a kit comprising the oligonucleotide of Claim 35 and an oligonucleotide comprising SEQ ID NO:2. The combination of the two oligonucleotides is not found in nature, because at least one of them is not found in nature. Therefore, Claims 20, 35 and 36 meet the requirement under 35 U.S.C. § 101.

Rejection of Claims 16, 18, 22, 23, 25, and 29 under 35 U.S.C. § 102(b)

Claims 16, 18, 22, 23, 25 and 29 were rejected under 35 U.S.C. § 102(b) as being anticipated by Weimer (U.S. Patent No. 6,248,526).

Regarding Claim 16, the Examiner stated that "Weimer teaches a kit for detecting HCV-1 in a sample comprising a primer that specifically anneals to the 5' noncoding region (see

Example 1 at column 6, lines 1-29, where SEQ ID NO: 1-3 taught by Weimer anneal to the 5' noncoding region of HCV)." See page 4, lines 6-8, of the Office Action.

Claim 16, as amended, is reproduced below:

> A kit for detecting HCV genotype 1 (HCV-1) in a sample, comprising at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome. (emphasis added)

Sequences of the primers taught by Weimer and referenced by the Examiner are reproduced below:

> SEQ ID NO:1 gcgtctagccatggcgttagt
> SEQ ID NO:2 ccacaaggcctttcgcgacccaacttact
> SEQ ID NO:3 ccacaaggcctttcgcgacccaacttact

The Examiner acknowledges at the last two lines on page 4 of the Office Action that "SEQ ID NO: 1 of Weimer is a universal primer suitable for isolating HCV from all HCV genotypes." Therefore, SEQ ID NO:1 of Weimer does not anneal specifically to the 5' NCR of the HCV-1 genome, but to all HCV genotypes.

SEQ ID NOs:2 and 3 of Weimer have the same nucleotide sequence. The first 24 nucleotides of this sequence anneal to all HCV genotypes. Applicant attaches hereto, as Exhibit A, example results of BLAST searches, showing 100% identity between the first 24 nucleotides of SEQ ID NO:2 or 3 and each genotype of HCV. The last 5 nucleotides of SEQ ID NO:2 or 3 are not complementary to the target nucleic acid and remain unpaired (see column 5, lines 20-22, of Weimer). Therefore, neither of SEQ ID NOs:2 and 3 of Weimer anneals specifically to the 5' NCR of the HCV-1 genome.

In summary, Weimer does not teach a primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome, as recited in Claim 16. Therefore, Claim 16, as amended, is not anticipated by Weimer under 35 U.S.C. § 102(b).

Because Claim 16 is not anticipated by Weimer under 35 U.S.C. § 102(b), Claims 22, 23, 25 and 29, which are dependent on Claim 16, are not anticipated by Weimer under 35 U.S.C. § 102(b), either.

Regarding Claim 18, the Examiner stated that "Weimer teaches an oligonucleotide suitable for use in an amplification reaction comprising SEQ ID NO:3."

Claim 18 has been amended to delete SEQ ID NO:3, thereby obviating the rejection.

Rejection of Claim 18 under 35 U.S.C. § 102(b)

Claim 18 was rejected under 35 U.S.C. § 102(b) as being anticipated by Hong *et al.* (WO 02/08447).

The Examiner stated that "Hong teaches an oligonucleotide comprising the instant SEQ ID NO:2."

Claim 18 has been amended to delete SEQ ID NO:2, thereby obviating the rejection.

Rejection of Claims 19 and 24 under 35 U.S.C. § 103(a)

Claims 19 and 24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Hong *et al.*

The Examiner stated: "The teachings of Weimer anticipates the instant claims 16, 18, 22, 23, 25, and 29. The teachings of Hong anticipates the instant claim 18." See page 6, lines 3-5, of the Office Action.

As discussed in the previous two sections, Claims 16, 28, 22, 23, 25 and 29, as amended, are not anticipated by the teachings of Weimer. Claim 18, as amended, is not anticipated by the teachings of Hong *et al.*

The Examiner stated, "SEQ ID NO: 1 of Weimer comprises the instant SEQ ID NO: 3," and that "Hong teaches a primer comprising the instant SEQ ID NO: 2 for amplification of HCV." The Examiner also stated, "It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to obtain a primer pair comprising an oligonucleotide of SEQ ID NO: 2 and an oligonucleotide of SEQ ID NO: 3." See page 6, lines 8-18, of the Office Action. The Examiner further stated: "Thus, the primer pair of claim 19 and the kit of claim 24 are prima facie obvious in view of the combined teachings of Weimer and Hong." See page 7, lines 8-10, of the Office Action.

Claim 19, which is directed to primer pairs, has been amended to delete the primer pair comprising nucleotide molecules having the sequences of SEQ ID NOs: 2 and 3, respectively, thereby obviating the rejection.

Claim 24 is dependent from Claim 23, which is in turn dependent from Claim 16. Claim 24 requires the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome," which is recited in Claim 16. This

limitation is not taught or suggested in either Weimer or Hong *et al.* Even if a person of ordinary skill in the art would have been motivated to combine Weimer and Hong *et al.* to use SEQ ID NOs:2 and 3 together as a primer pair for specific amplification of HCV, the combination of the teachings of Weimer and Hong *et al.* does not teach or suggest an essential element of Claim 24, i.e., "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome." "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." U.S. DEP'T OF COM., U.S. PATENT & TRADEMARK OFFICE, THE MANUAL OF PATENT EXAMINING PROCEDURE (2007) (hereinafter "the MPEP"), § 2143.03. Therefore, the invention of Claim 24 is not obvious under 35 U.S.C. § 103(a) over Weimer in view of Hong *et al.*

Rejection of Claim 20 under 35 U.S.C. § 103(a)

Claim 20 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Bukh *et al.* (Proceedings of the National Academy of Sciences, USA (1992) 89(11):4942-4946) in view of Watanabe *et al.* (Journal of Microbiological Methods (2001) 44:253-262) and further in view of Heid *et al.* (Genome Research (1996) 6(10):986-994).

Bukh *et al.* teaches an alignment of nucleotide sequences of the 5' NCR of 44 HCV isolates from around the world. These sequences are compared to a prototype HCV sequence (HCV1). See FIG. 1 legend on page 4943.

Watanabe *et al.* teaches introduction of deoxyinosines at nucleotide positions where mismatches occur in any sequence in an alignment. See page 258.

Heid *et al.* teaches an oligonucleotide probe labeled at the 5' end with FAM and the 3' end with TAMRA for detection of PCR products. See page 987, column 2 and page 993, column 1.

The Examiner stated that the complement of nucleotides -93 to -69 in the prototype HCV-1 sequence of the 5' NCR taught in Bukh *et al.* is highly similar to the claimed SEQ ID NO:6. See page 7, lines 16-18, of the Office Action. The Examiner also stated: "It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to synthesize a probe comprising SEQ ID NO:6. ... An ordinary practitioner also would have been motivated to substitute inosine at those nucleotide positions where variability was observed, ... An

ordinary practitioner would have been motivated to substitute inosine at the claimed positions in SEQ ID NO:6, since the alignment of Bukh showed sequence variability at these positions (see Figure 1). Finally, an ordinary practitioner would have been motivated to label the probe with FAM and TAMRA to permit its use in quantitative real-time PCR as suggested by Heid." See page 8, line 21 through page 9, line 14, of the Office Action.

SEQ ID NO:6 has been amended in a Substitute Sequence Listing being filed concurrently herewith, to delete the last "T" from the sequence, which denotes TAMRA labeling instead of deoxythymidine.

The complement of nucleotides -92 to -69 in the 5' NCR of the prototype HCV1 sequence of Bukh *et al.* is aligned with the amended SEQ ID NO:6 below:

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Bukh HCV1        -69  CGCGACCCAACACTACTCGGCTAG -92
                      ||| ||||||| ||||| ||||||
SEQ ID NO:6      1    CGCIACCCAACICTACTIGGCTAG 24
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As shown in this alignment, there are three positions in the Bukh *et al.* sequence where inosine is substituted in SEQ ID NO:6, namely, positions -72, -80 and -86 of the Bukh *et al.* HCV1 sequence. However, these are not the only positions where mismatch occurred in the sequence of -69 to -92 of HCV1 in the alignment in FIG. 1 of Bukh *et al.* Referring to FIG. 1 of Bukh *et al.*, a mismatch also occurred at position -91. Compare the HCV1 sequence and the Z1 sequence in the alignment shown in FIG. 1, where the nucleotide at position -91 is T for HCV1 and C for Z1. SEQ ID NO:6 does not have inosine substitution at this position. Therefore, there is at least one position of mismatch wherein the inosine substitution is avoided according to the present invention.

Watanabe *et al.* teaches introduction of deoxyinosines at nucleotide positions where mismatches occur in any sequence in an alignment. It does not teach or suggest, for positions where mismatches occur, under what conditions the introduction of deoxyinosine should be avoided, as it was at position 23 of SEQ ID NO:6. The combination of the teachings of Bukh *et al.*, Watanabe *et al.* and Heid *et al.* does not teach or suggest this either. Bukh *et al.*, Watanabe *et al.* and Heid *et al.* do not teach or suggest, either individually or in combination, the claimed invention. Therefore, the invention of Claim 20 is not obvious under 35 U.S.C. § 103(a) over Bukh *et al.* in view of Watanabe *et al.* and further in view of Heid *et al.*

Rejection of Claim 27 under 35 U.S.C. § 103(a)

Claim 27 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Buck *et al.* (Biotechniques (1999) 27(3):528-536).

The teachings of Weimer, Bukh *et al.* and Watanabe *et al.* have been discussed above. Watanabe *et al.* teaches introduction of deoxyinosines at nucleotide positions where mismatches occur in any sequence in an alignment for the purpose of improving annealing of primers to genetically diverse bacterial populations, i.e., to improve the usefulness of primers as universal primers for amplification. The teachings of Weimer do not anticipate the products of Claims 16, 18, 23, 25 and 29, as discussed above.

Buck *et al.* analyzed the effect of primer design strategy on the performance of DNA sequencing primers in an automated DNA sequencing system using AmpliTaq® reagents. The authors concluded that "nearly all of the primers yielded data of extremely high quality."

Claim 27 is dependent from Claim 16 and requires the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome," which is recited in Claim 16. Claim 27 further limits this limitation to SEQ ID NO:1, which anneals specifically to the 5' NCR of the HCV-1 genome.

Bukh *et al.* teaches that the "long stretches of invariant nucleotides are preferred for primer design," and that the "variable sequences within the 5' NC region of the HCV genome ... should be avoided in the design of primers." See page 4946, left column, lines 28-36. The region in the 5' NCR of the HCV1 sequence in Bukh *et al.* that corresponds to SEQ ID NO:1 (i.e., nucleotides -134 to -118 of the HCV1 sequence in Bukh *et al.*) is among the most variable sequences within the 5' NCR of the HCV genome. See FIG. 1 on page 4943. Therefore, Bukh *et al.* specifically teaches away from choosing this region in the design of primers.

In addition, there is only one inosine substitution in SEQ ID NO:1. This is in contrast to the eight variable positions in nucleotides -134 to -118 of the HCV1 sequence in Bukh *et al.*, namely, positions -118, -119, -121, -122, -124, -125, -128 and -132 of the HCV1 sequence in Bukh *et al.* See FIG. 1 on page 4943. Therefore, there are seven out of eight positions of mismatch in this region wherein the inosine substitution is avoided according to the present invention.

As discussed above, Watanabe *et al.*, does not teach or suggest, for positions where mismatches occur, under what conditions the introduction of deoxyinosine should be avoided.

In summary, the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome" is not taught or suggested in any of Weimer, Bukh *et al.*, Watanabe *et al.*, and Buck *et al.*, or any combinations thereof. None of these references, or any combinations thereof, teach or suggest, for positions where mismatches occur, under what conditions the introduction of deoxyinosine should be avoided. In addition, Bukh *et al.* specifically teaches away from the claimed invention. The combined teachings of Weimer, Bukh *et al.*, Watanabe *et al.*, and Buck *et al.* do not teach or suggest the kit of claim 27. Therefore, the invention of Claim 27 is not obvious over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Buck *et al.*

Rejection of Claims 19 and 28 under 35 U.S.C. § 103(a)

Claims 19 and 28 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Buck *et al.*, and further in view of Hong *et al.*

The teachings of Weimer, Bukh *et al.*, Watanabe *et al.* and Buck *et al.* have been discussed above. As discussed above, the teachings of Weimer do not anticipate the products of Claims 16, 18, 23, 25 and 29, and the combined teachings of Weimer, Bukh *et al.*, Watanabe *et al.*, and Buck *et al.* do not result in the kit of claim 27.

Hong *et al.* teaches nucleic acids and methods for detecting viral infection, uncovering anti-viral drug candidates and determining drug resistance of viral isolates. See the claims of Hong *et al.* Hong *et al.* does not teach or suggest a primer comprising SEQ ID NO: 1

The Examiner stated that "the combined teachings of Bukh and Watanabe suggest a primer comprising SEQ ID NO: 1." See page 14, lines 10-11, of the Office Action. The Examiner also stated, "It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to obtain a primer pair comprising an oligonucleotide of SEQ ID NO: 1 and an oligonucleotide of SEQ ID NO:2." See page 14, lines 18-20, of the Office Action.

Applicant respectfully disagrees. As discussed in the previous section, there is only one inosine substitution in SEQ ID NO:1, but eight variable positions in nucleotides -134 to -118 of

the HCV1 sequence in Bukh *et al.* Therefore, there are seven out of eight positions of mismatch in this region wherein the inosine substitution is avoided according to the present invention. Because Watanabe *et al.*, does not teach or suggest, for positions where mismatches occur, under what conditions the introduction of deoxyinosine should be avoided, the combination of the teachings of Bukh *et al.* and Watanabe *et al.* does not teach or suggest a primer comprising SEQ ID NO: 1.

None of Weimer, Buck *et al.* and Hong *et al.*, or any combinations thereof, teach or suggest a primer comprising SEQ ID NO: 1. Weimer, Buck *et al.* and Hong *et al.* do not make up for the deficiency of Bukh *et al.* and Watanabe *et al.* Therefore, none of Weimer, Bukh *et al.*, Watanabe *et al.*, Buck *et al.*, and Hong *et al.*, or any combinations thereof, teach or suggest a primer comprising SEQ ID NO: 1.

Because none of Weimer, Bukh *et al.*, Watanabe *et al.*, Buck *et al.*, and Hong *et al.*, or any combinations thereof, teach or suggest a primer comprising SEQ ID NO: 1, none of these references or any combinations thereof teach or suggest a primer pair comprising SEQ ID NO:1, e.g., a primer pair comprising an oligonucleotide of SEQ ID NO: 1 and an oligonucleotide of SEQ ID NO:2. Therefore, the inventions of Claims 19 and 28 are not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Buck *et al.*, and further in view of Hong *et al.*

Rejection of Claim 30 under 35 U.S.C. § 103(a)

Claim 30 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Heid *et al.*

The teachings of Weimer, Bukh *et al.*, Watanabe *et al.*, and Heid *et al.* have been discussed above. The teachings of Weimer do not anticipate the products of Claims 16, 18, 23, 25 and 29, as discussed above.

Claim 30 is dependent from Claim 29, which, in turn, is dependent from Claim 16. Claim 30 requires the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome," which is recited in Claim 16. As discussed above, such limitation is not taught or suggested in any of Weimer, Bukh *et al.*, Watanabe *et al.*, and Heid *et al.*, or any combinations thereof. "To establish *prima facie* obviousness of a claimed

invention, all the claim limitations must be taught or suggested by the prior art." See the MPEP § 2143.03. Therefore, the invention of Claim 30 is not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.*, in view of Watanabe *et al.*, and further in view of Heid *et al.*

Rejection of Claims 31 and 32 under 35 U.S.C. § 103(a)

Claims 31 and 32 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.* and further in view of Tyagi *et al.* (U.S. Patent No. 6,037,130) and further in view of Buck *et al.*

The teachings of Weimer, Bukh *et al.*, and Buck *et al.* have been discussed above. The teachings of Weimer do not anticipate the products of Claims 16, 18, 23, 25 and 29, as discussed above.

Tyagi *et al.* teaches wavelength-shifting molecular beacon primers. See column 2, lines 29-44, of Tyagi *et al.* Tyagi *et al.* does not teach or suggest any primer or probe that anneals specifically to the 5' NCR of the HCV-1 genome.

Claim 31 is dependent from Claim 16. Claim 32 is dependent from Claim 31. Both Claims 31 and 32 require the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome," which is recited in Claim 16. As discussed above, such limitation is not taught or suggested in any of Weimer, Bukh *et al.*, and Buck *et al.*, or any combinations thereof. Such deficiency is not made up by Tyagi *et al.* "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." See the MPEP § 2143.03. Therefore, the inventions of Claims 31 and 32 are not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.* and further in view of Tyagi *et al.* and further in view of Buck *et al.*

Rejection of Claims 19 and 33 under 35 U.S.C. § 103(a)

Claims 19 and 33 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.* and further in view of Tyagi *et al.* and further in view of Buck *et al.* and further in view of Hong *et al.*

The teachings of Weimer, Bukh *et al.*, Tyagi *et al.*, Buck *et al.* and Hong *et al.* have been discussed above. The teachings of Weimer do not anticipate the products of Claims 16, 18, 23,

25 and 29, and the combined teachings of Weimer, Bukh *et al.*, Tyagi *et al.*, and Buck *et al.* do not result in the kit of Claims 31 and 32, as discussed above.

Regarding Claim 19, the Examiner stated that "the combined teachings of Bukh and Tyagi suggest a primer comprising SEQ ID NO: 7." See page 23, lines 8-9, of the Office Action. The Examiner also stated that "It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to obtain a primer pair comprising an oligonucleotide of SEQ ID NO: 7 and an oligonucleotide of SEQ ID NO: 2." See page 23, lines 16-18, of the Office Action.

Applicant respectfully disagrees.

The Examiner stated that "the hairpin region of the molecular beacon primer taught by Tyagi exactly matches the 5' portion of the claimed sequence (see column 18, where SEQ ID NO: 12 of Tyagi contains the sequence 5'-FAM-caccttcaccctcagaagg-DABCYL-g)." See page 20, lines 2-4, of the Office Action.

SEQ ID NO:12 of Tyagi *et al.* is the sequence of primer F, in which "[a]t least the first eighteen nucleotides from the 3' end were complementary to a target." See column 18, lines 40-55, of Tyagi *et al.*

There are only seventeen nucleotides to the 3' of the 5'-FAM-caccttcaccctcagaagg-DABCYL-g sequence in SEQ ID NO:7, namely CCGCTCAATGCCTGGAG. By requiring at least eighteen nucleotides from the 3' end to such sequence, Tyagi *et al.* actually teaches away from a primer comprising SEQ ID NO:7. Therefore, the combined teachings of Bukh *et al.* and Tyagi *et al.* do not teach or suggest a primer comprising SEQ ID NO:7.

None of Weimer, Buck *et al.* and Hong *et al.*, or any combinations thereof, teach or suggest a primer comprising SEQ ID NO:7. Weimer, Buck *et al.* and Hong *et al.* do not make up for the deficiency of Bukh *et al.* and Tyagi *et al.* Therefore, none of Weimer, Bukh *et al.*, Tyagi *et al.*, Buck *et al.* and Hong *et al.*, either individually or in combination, teach or suggest a primer comprising SEQ ID NO:7.

Because none of Weimer, Bukh *et al.*, Tyagi *et al.*, Buck *et al.* and Hong *et al.* teach or suggest a primer comprising SEQ ID NO:7, none of these references, or any combinations thereof, teach or suggest a primer pair comprising an oligonucleotide of SEQ ID NO: 7, e.g., a primer pair comprising an oligonucleotide of SEQ ID NO:7 and an oligonucleotide of SEQ ID

NO: 2. Therefore, the invention of Claim 19, as amended, is not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.* and further in view of Tyagi *et al.* and further in view of Buck *et al.* and further in view of Hong *et al.*

Claim 33 is dependent from Claim 32, which is dependent from Claim 31, which, in turn, is dependent from Claim 16. Claim 33 requires the limitation of "at least one primer or probe that anneals specifically to the 5' noncoding region (5' NCR) of the HCV-1 genome," which is recited in Claim 16. As discussed above, such limitation is not taught or suggested in any of Weimer, Bukh *et al.*, Tyagi *et al.*, Buck *et al.* and Hong *et al.*, or any combinations thereof. "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." See the MPEP § 2143.03. Therefore, the invention of Claim 33 is not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.* and further in view of Tyagi *et al.* and further in view of Buck *et al.* and further in view of Hong *et al.*

Rejection of Claim 35 under 35 U.S.C. § 103(a)

Claim 35 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Bukh *et al.* in view of Tyagi *et al.*

The teachings of Bukh *et al.* and Tyagi *et al.* have been discussed above.

Claim 35, as amended recites "An isolated and purified oligonucleotide comprising SEQ ID NO:7."

As discussed in the previous section, the combined teachings of Bukh *et al.* and Tyagi *et al.* do not teach or suggest a primer comprising SEQ ID NO:7. Therefore, the invention of Claim 35, as amended, is not obvious over Bukh *et al.* in view of Tyagi *et al.*

Rejection of Claim 36 under 35 U.S.C. § 103(a)

Claim 36 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Weimer in view of Bukh *et al.*, in view of Tyagi *et al.*, and further in view of Hong *et al.*

The teachings of Weimer, Bukh *et al.*, Tyagi *et al.* and Hong *et al.* have been discussed above.

Claim 36 is dependent from Claim 35.

The combined teachings of Bukh *et al.* and Tyagi *et al.* do not result in the oligonucleotide of Claim 35, as discussed in the preceding two sections. Neither Weimer nor Hong *et al.*, nor a combination thereof, teach or suggest the oligonucleotide of Claim 35. Weimer and Hong *et al.* do not make up for the deficiency of Bukh *et al.* and Tyagi *et al.* Therefore, Claim 35 is patentable under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.*, in view of Tyagi *et al.*, and further in view of Hong *et al.*

Because the invention of Claim 35 is not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.*, in view of Tyagi *et al.*, and further in view of Hong *et al.*, and because Claim 36 is dependent from Claim 35, the invention of Claim 36 is also not obvious under 35 U.S.C. § 103(a) over Weimer in view of Bukh *et al.*, in view of Tyagi *et al.*, and further in view of Hong *et al.*

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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